#9

FORM PTO-1449 (Modified)	ATTY. DOCKET NO. 37851-0911	SERIAL NO. 10/022,249
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT	APPLICANT VEGA et al.	
	FILING DATE December 17, 2001	GROUP ~~1643~~ 1631

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB CLASS	FILING DATE
CSM	A	4 7 9 7 3 6 8	01/10/89	Carter *et al.*	435	320	03/15/85
	B	5 1 3 9 9 4 1	08/18/92	Muzyczka *et al.*	435	172.3	10/25/91
	C	5 5 7 1 6 9 8	11/05/96	Ladner *et al.*	435	69.7	06/18/93
	D	5 7 2 3 3 2 3	03/03/98	Kauffman *et al.*	435	172.3	12/02/94
	E	5 7 5 3 5 0 0	05/19/98	Shenk *et al.*	435	320.1	04/03/95
	F	5 7 6 3 2 3 9	06/09/98	Short *et al.*	435	172.1	06/18/96
	G	5 7 7 0 4 3 4	06/23/98	Huse	435	252.33	05/15/95
	H	5 7 7 9 4 3 4	07/14/98	De Long	415	104	02/06/97
	I	5 7 9 8 3 9 0	08/25/98	Weber *et al.*	514	634	05/22/95
	J	5 8 3 7 5 0 0	11/17/98	Ladner *et al.*	435	69.7	04/03/95
	K	5 8 6 2 5 1 4	01/19/99	Huse *et al.*	702	22	12/06/96
	L	5 8 7 1 9 7 4	02/16/99	Huse	435	69.7	12/02/94
	M	6 0 0 1 5 7 4	12/14/99	Short *et al.*	435	6	03/04/98
	N	6 0 5 7 1 0 3	05/02/00	Short	435	6	08/26/97
	O	6 0 9 6 5 4 8	08/01/00	Stemmer	435	440	02/03/97
	P	6 1 1 7 6 7 9	09/12/00	Stemmer	435	440	05/25/96
	Q	6 1 2 7 1 7 5	10/03/00	Vigne *et al.*	435	325	07/17/97
	R	6 1 3 2 9 7 0	10/17/00	Stemmer	435	6	06/19/98
	S	6 1 5 6 5 0 9	12/05/00	Schellenberger	435	6	11/12/97
	T	6 1 6 5 7 9 3	12/26/00	Stemmer	435	440	05/08/98
	U	6 1 7 1 8 2 0	01/09/01	Short	435	69.1	02/04/99
	V	6 1 7 4 6 7 3	01/16/01	Short *et al.*	435	6	06/16/98
	W	6 1 8 0 4 0 6	01/30/01	Stemmer	435	440	06/17/98
	X	6 2 3 8 8 8 4	05/29/01	Short *et al.*	435	69.1	03/09/99

EXAMINER C. Murphy | DATE CONSIDERED October 22, 2002

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Title: **HIGH THROUGHPUT DIRECTED EVOLUTION BY RATIONAL MUTAGENESIS**

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CSM	Y	6	2	5	8	5	3	0	07/10/01	Huse	435	6	12/30/94

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER							DATE	COUNTRY	CLASS	SUB CLASS	Translation Yes	Translation No
CSM	Z	0	1	4	4	8	0	9	06/21/01	PCT	—	—	X	
	AA	0	1	8	6	2	9	1	11/15/01	PCT	—	—		X*
	AB	9	9	1	1	7	6	4	03/11/99	PCT	—	—		
↓	AC	2	8	0	2	6	4	5	12/16/99	FR	—	—		X*

X* = An English Language Derwent Abstract is Provided.

OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

CSM	AD	Ashktorab *et al.*, "Identification of Nuclear Proteins That Specifically Interact with Adeno-Associated Virus Type 2 Inverted Terminal Repeat Hairpin DNA", *Journal of Virology*, 63:3034-3039 (1989)
	AE	ATCC accession no. VR-646, "Adeno-associated virus 4 deposited as Adeno-associated virus type 4", (accessed on 09/05/2002)
	AF	ATCC accession no. VR-1449, "Simian virus 15", (accessed on 09/05/2002)
	AG	ATCC accession no. VR-680, "Adeno-associated virus 2 deposited as Adeno-associated virus type 2", (accessed on 09/05/2002)
	AH	ATCC accession no. VR-681, "Adeno-associated virus 3 deposited as Adeno-associated virus type 3", (accessed on 09/05/2002)
	AI	ATCC accession no. VR-645, "Adeno-associated virus 1 deposited as Adeno-associated (satellite) virus type 1", (accessed on 09/05/2002)
	AJ	Atkinson *et al.*, "A high-throughput hybridization method for titer determination of viruses and gene therapy vectors", *Nucleic Acids Research.*, 26:2821-2823 (1998)
↓	AK	Altschul *et al.*, "Basic Local Alignment Search Tool", *J. Molec. Biol.*, 215:403-410 (1990)

EXAMINER C. Meucci | DATE CONSIDERED October 12, 2004

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CSW	AL	Batchu *et al.*, "Disassociation of Conventional DNA Binding and Endonuclease Activities by an Adeno-Associated Virus Rep78 Mutant", *Biochemical And Biophysical Research Communications*, 210:717-725 (1995)
	AM	Beaton *et al.*, "Expression from the Adeno-Associated Virus p5 and p19 Promoters Is Negatively Regulated in *trans* by the *rep* Protein", *Journal of Virology*, 63:4450-4454 (1989)
	AN	Beck-Sickinger *et al.*, "Complete L-alanine scan of neuropeptide Y reveals ligands binding to Y_1 and Y_2 receptors with distinguished conformations", *Eur. J. Biochem.*, 223:947-958 (1994)
CARRILLO	AO	~~Carillo~~ *et al.*, "The Multiple Sequence Alignment Problem in Biology", *SIAM J. Applied Math*, 48:1073-1082 (1988)
	AP	Cassinotti *et al.*, "Organization of the Adeno-Associated Virus (AAV) Capsid Gene: Mapping of a Minor Spliced mRNA Coding for Virus Capsid Protein 1", *Virology*, 167:176-184 (1988)
	AQ	Chadeuf *et al.*, "Efficient recombinant adeno-associated virus production by a stable rep-cap HeLa cell line correlates with adenovirus-induced amplification of the integrated rep-cap genome", *J. Gene Med.*, 2:260-268 (2000)
	AR	Chejanovsky *et al.*, "Mutation of a Consensus Purine Nucleotide Binding Site in the Adeno-Associated Virus *rep* Gene Generates a Dominant Negative Phenotype for DNA Replication", *J. Virology*, 64:1764-1770 (1990)
	AS	Chejanovsky *et al.*, "Mutagenesis of an AUG Codon in the Adeno-Associated Virus *rep* Gene: Effects on Viral DNA Replication", *J. Virology*, 173:120-128 (1989)
	AT	Cullen *et al.*, "Analysis of the Physical State of Different Human Papillomavirus DNAs in Intraepithelial and Invasive Cervical Neoplasm", *Journal of Virology*, 65:606-612 (1991)
	AU	Davis *et al.*, "Mutational Analysis of Adeno-Associated Virus Type 2 Rep68 Protein Endonuclease Activity on Partially Single-Stranded Substrates", *Journal of Virology*, 74:2936-2942 (2000)
	AV	Davis *et al.*, "Analysis of the Effects of Charge Cluster Mutations in Adeno-Associated Virus Rep68 Protein In Vitro", *Journal of Virology*, 73:2084-2093 (1999)
√	AW	Deng *et al.*, "Site-Directed Mutagenesis of Virtually Any Plasmid by Eliminating a Unique Site", *Analytical Biochemistry*, 200:81-88 (1992)

EXAMINER C. Min | DATE CONSIDERED October 12, 2004

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OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

CJM		AX	Derwent # 013914049, WPI Acc. No. 2001-398262/200142, for French Patent FR 2802645 and PCT Patent Application WO 2001/44809 "Evaluating the performance of complex biological agents in target cells, for selecting gene therapy vectors with optimal properties, comprises constructing a theoretical curve"
		AY	Derwent # 014262217, WPI Acc. No. 2002-082915/200211, for PCT Patent Application WO 2001/86291 A1, "Determining titer of biological agent, useful e.g. for gene therapy vectors or vaccines, is based on measuring reaction with cells at constant concentration, over a specified time period"
		AZ	Devereux *et al.*, "A comprehensive set of sequence analysis programs for the VAX", *Nucleic Acids Research*, 12(I):387-395 (1984)
		BA	Drittanti *et al.*, "High throughput production, screening and analysis of adeno-associated viral vectors", *Gene Therapy*, 7:924-929 (2000)
		BB	Drittanti *et al.*, "Optimised helper virus-free production of high-quality adeno-associated virus vectors", *The Journal of Gene Medicine*, 3:59-71 (2001)
		BC	Du *et al.*, "Efficient transduction of human neurons with an adeno-associated virus vector", *Gene Therapy*, 3:254-261 (1996)
		BD	Gavin *et al.*, "Charge-to-Alanine Mutagenesis of the Adeno-Associated Virus Type 2 Rep78/68 Proteins Yields Temperature-Sensitive and Magnesium-Dependent Variants", *Journal of Virology*, 73:9433-9445 (1999)
		BE	Genbank accession no. NC_002077, Nucleotide, "Adeno-associated virus 1, complete genome", (accessed on 09/05/2002)
		BF	Genbank accession no. NC_001829, Nucleotide, "Adeno-associated virus 4, complete genome", (accessed on 09/05/2002)
		BG	Genbank accession no. NC_001863, Nucleotide, "Adeno-associated virus 3B, complete genome", (accessed on 09/05/2002)
		BH	Genbank accession no. NC_001401, Nucleotide, "Adeno-associated virus 2, complete genome", (accessed on 09/05/02)
		BI	Genbank accession no. NC_001729, Nucleotide, "Adeno-associated virus 3, complete genome", (accessed on 09/05/02)
✓		BJ	Gibbs *et al.*, "Rational Scanning Mutagenesis of a Protein Kinase Identifies Functional Regions Involved in Catalysis and Substrate Interactions", *Journal of Biology Chemistry*, 266:8923-8931 (1991)

EXAMINER C. Mahl | DATE CONSIDERED October 2, 2004

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OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

CJM	BK	Gribskov *et al.*, "Sigma factors from *E. coli, B. subtilis,* phage SP01, and phage T4 are homologous proteins", *Nucleic Acids Research*, 14:6745-6763 (1986)
	BL	Hermonat, P.L., "Down-regulation of the human c-*fos* and c-*myc* proto-oncogene promoters by adeno-associated virus Rep78", *Cancer Letters*, 81:129-136 (1994)
	BM	Hermonat *et al.*, "Genetics of Adeno-Associated Virus: Isolation and Preliminary Characterization of Adeno-Associated Virus Type 2 Mutants", *Journal of Virology*, 51:329-339 (1984)
	BN	Hill A.V., "The possible effects of the aggregation of the molecules of haemoglobin on its dissociation curves", *Proceedings of the Physiological, Journal of Physiology*, 40:iv-vii (1910)
	BO	Hill *et al.*, "XLVII. The Combinations Of Haemoglobin With Oxygen And With Carbon Monoxide", *I. Biochem. J.*, 7:471-480 (1913)
	BP	Horer *et al.*, "Mutational Analysis of Adeno-Associated Virus Rep Protein-Mediated Inhibition of Heterologous and Homologous Promoters", *Journal of Virology*, 69:5485-5496 (1995)
	BQ	Im *et al.*, "Partial Purification of Adeno-Associated Virus Rep78, Rep52, and Rep40 and Their Biochemical Characterization", *Journal of Virology*, 66:1119-1128 (1992)
	BR	Im *et al.*, "The AAV Origin Binding Protein Rep68 Is an ATP-Dependent Site-Specific Endonuclease with DNA Helicase Activity", *Cell*, 61:447-457 (1990)
	BS	Kechli *et al.*, "Expression of the Human Immunodeficiency Virus Type 1 Primer Binding Sequence Inhibits HIV-1 Replication", *Human Gene Therapy*, 9:587-590 (1998)
	BT	Kyostio *et al.*, "Negative Regulation of the Adeno-Associated Virus (AAV) P_5 Promoter Involves both the P_5 Rep Binding Site and the Consensus ATP-Binding Motif of the AAV Rep68 Protein", *Journal of Virology*, 69:6787-6796 (1995)
	BU	Kyostio *et al.*, "Identification of Mutant Adeno-Associated Virus Rep Proteins Which Are Dominant-Negative For DNA Helicase Activity", *Biochemical and Biophysical Research Communications*, 220:294-299 (1996)
	BV	Kyostio *et al.*, "Analysis of Adeno-Associated Virus (AAV) Wild-Type and Mutant Rep Proteins for Their Abilities To Negatively Regulate AAV p_5 and p_{19} mRNA Levels", *Journal of Virology*, 68:2957-2957 (1994)
✓	BW	Marcello *et al.*, "Adeno-Associated Virus Type 2 Rep Protein Inhibits Human Papillomavirus Type 16 E2 Recruitment of the Transcriptional Coactivator p300", *Journal of Virology*, 74:9090-9098 (2000)

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C4M	BX	Matsushita *et al.*, "Localization of von Willebrand Factor-binding Sites for Platelet Glycoprotein Ib and Botrocetin by Charged-to-Alanine Scanning Mutagenesis", *Journal of Biology Chemistry*, 275:11044-11049 (2000)
	BY	McCarty *et al.*, "Analysis of Mutations in Adeno-Associated Virus Rep Protein In Vivo and In Vitro", *Journal of Virology*, 66:4050-4057 (1992)
	BZ	Mendelson *et al.*, "Identification of the *trans*-Acting Rep Proteins of Adeno-Associated Virus by Antibodies to a Synthetic Oligopeptide", *Journal of Virology*, 60:823-832 (1986)
	CA	Mittereder *et al.*, "Evaluation of the Concentration and Bioactivity of Adenovirus Vectors for Gene Therapy", *Journal of Virology*, 70:7498-7509 (1996)
	CB	Needleman *et al.*, "A General Method Applicable to the Search for Similarities in the Amino Acid Sequence of Two Proteins", *Journal of Molec. Biol.*, 48:443 (1970)
	CC	Nelson *et al.*, "Characterization of Diverse Viral Vector Preparations, Using a Sample and Rapid Whole-Virion Dot-Blot Method", *Hum. Gene Ther.*, 9:2401-2405 (1998)
	CD	Ni *et al.*, "In Vitro Replication of Adeno-Associated Virus DNA", *Journal of Virology*, 68:1128-1138 (1994)
	CE	Owens *et al.*, "Identification of a DNA-Binding Domain in the Amino Terminus of Adeno-Associated Virus Rep Proteins," *J. Virology*, 67(2):997-1005 (1993)
	CF	Owens *et al.*, "In Vitro Resolution of Adeno-Associated Virus DNA Hairpin Termini by Wild-Type Rep Protein Is Inhibited by a Dominant-Negative Mutant of Rep", *Journal of Virology*, 66:1236-1240 (1992)
	CG	Owens *et al.*, "Adeno-Associated Virus Rep Proteins Produced in Insect and Mammalian Expression Systems: Wild-Type and Dominant-Negative Mutant Proteins Bind to the Viral Replication Origin", *Journal of Virology*, 184:14-22 (1991)
	CH	Pearson *et al.*, "Improved tools for biological sequence comparison", *Proc. Natl. Acad. Sci. USA*, 85:2444 (1988)
	CI	Press Release 11; "Nautilus Biotech granted patent covering molecular fitness analysis with key applications in directed evolution and functional genomics target identification"; Paris- February 6, 2002; http://www.nautilusbiotech.com/news-pressrelease11.php3, accessed on (2/28/02)
√	CJ	Press Release 10; "Nautilus Biotech and Microbix Biosystems, Inc. (TSE: MBX) sign a distribution agreement for rAAV high-producer cells"; Paris- January 11, 2002; http://www.nautilusbiotech.com/news-pressrelease10.php3, accessed on (2/28/02)

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CM	CK	Press Release 7; "Nautilus Biotech optimizes the AAV rep protein to increase rAAV productivity"; Paris- September 21, 2001; http://www.nautilusbiotech.com/news-pressrelease7.php3, accessed on (2/28/02)
	CL	Press Release 6; "Nautilus Biotech S.A. Files a Key Patent Application in the U.S."; Paris- September 14, 2001; http://www.nautilusbiotech.com/news-pressrelease6.php3, accessed on (2/28/02)
	CM	Ropp *et al.*, "*Aequorea* Green Fluorescent Protein Analysis by Flow Cytometry", *Cytometry*, 21:309-317 (1995)
	CN	Ruffing *et al.*, "Mutations in the carboxy terminus of adeno-associated virus 2 capsid proteins affect viral infectivity: lack of an RGD integrin-binding motif", *J. Gen. Virol.*, 75:3385-3392 (1994)
	CO	Ryan *et al.*, "Sequence Requirements for Binding of Rep68 to the Adeno-Associated Virus Terminal Repeats", *Journal of Virology*, 70:1542-1553 (1996)
	CP	Salvetti *et al.*, "Factors Influencing Recombinant Adeno-Associated Virus Production", *Hum. Gene Ther.*, 20:695-706 (1998)
	CQ	Samulski *et al.*, "A Recombinant Plasmid from Which an Infectious Adeno-Associated Virus Genome Can Be Excised In Vitro and Its Use To Study Viral Replication", *Journal of Virology*, 61:3096-3101 (1987)
	CR	Schwartz *et al.*, "Matrices for Detecting Distant Relationships", Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, pp. 353-358 (1978)
	CS	Smith *et al.*, "Comparison of Biosequences", *Advances in Applied Mathematics*, 2:482-489 (1981)
	CT	Smith *et al.*, "Single-step purification of polypeptides expressed in *Escherichia coli* as fusions with glutathione *S*-transferase", *Gene*, 67:31-40 (1988)
	CU	Srivastava *et al.*, "Nucleotide Sequence and Organization of the Adeno-Associated Virus 2 Genome", *Journal of Virology*, 45:555-564 (1983)
	CV	Tessier *et al.*, "Characterization of Adenovirus-Induced Inverted Terminal Repeat-Independent Amplification of Integrated Adeno-Associated Virus *rep-cap* Sequences", *Journal of Virology*, 75:375-383 (2001)
	CW	Translation of PCT Patent Application WO 01/44809, "Methods for Screening or Assessing the Performance of a Collection of Biological Agents in Living Parget Cells, And Their Applications"

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CHM	CX	Urabe *et al.*, "Charged-to-Alanine Scanning Mutagenesis of the N-Terminal Half of Adeno-Associated Virus Type 2 Rep78 Protein", *Journal of Virology*, 23:2682-2693 (1999)
	CY	Walker *et al.*, "Mutational Analysis of the Adeno-Associated Virus Type 2 Rep68 Protein Helicase Motifs", *Journal of Virology*, 71:6996-7004 (1997)
	CZ	Walker *et al.*, "Mutational Analysis of the Adeno-Associated Virus Rep68 Protein: Identification of Critical Residues Necessary for Site-Specific Endonuclease Activity", *Journal of Virology*, 71:2722-2730 (1997)
	DA	Watson *et al.*, "*Molecular Biology of the Gene*", 4th Ed., The Benjamin/Cummings Pub. Co., p. 224, (1987)
	DB	Weitzman *et al.*, "Interaction of Wild-Type and Mutant Adeno-Associated Virus (AAV) Rep Proteins on AAV Hairpin DNA", *Journal of Virology*, 70:2240-2248 (1996)
	DC	Weitzman *et al.*, "Recruitment of Wild-Type and Recombinant Adeno-Associated Virus into Adenovirus Replication Centers", *Journal of Virology*, 70:1845-1854 (1996)
	DD	Wu *et al.*, "Mutational Analysis of the Adeno-Associated Virus Type 2 (AAV2) Capsid Gene and Construction of AAV2 Vectors with Altered Tropism", *J. Virol.*, 74:8635-8647 (2000)
	DE	Yang *et al.*, "Mutational Analysis of the Adeno-Associated Virus *rep* Gene", *Journal of Virology*, 66:6058-6069 (1992)
	DF	Yang *et al.*, "Analysis of the Terminal Repeat Binding Abilities of Mutant Adeno-Associated Virus Replication Proteins", *Journal of Virology*, 67: 4442-4447 (1993)
✓	DG	Yoon *et al.*, "Amino-Terminal Domain Exchange Redirects Origin-Specific Interactions of Adeno-Associated Virus Rep78 In Vitro", *Journal of Virology*, 75:3230-3239 (2001)

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